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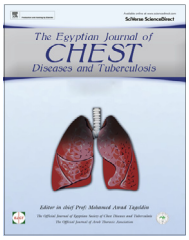

EDITORIAL

Obesity and lung health

Obesity among population has increased dramatically and has received considerable recent public health attention. The impact of obesity on lung health has become a recognized problem worldwide and an area of intense research. Obese people are at greater risk for asthma, impaired lung mechanics, sleep-disordered breathing, and obesity hypoventilation syndrome.

Complete pulmonary function testing (measuring spirometry, lung volumes, and diffusion) often shows a restrictive disease pattern with decreased expiratory reserve volume (ERV) and functional residual capacity (FRC). For more information on pulmonary function testing, see http://www.nlm.nih.gov/medlineplus/ency/article/003853.htm. (Also see *Guide* to respiratory abbreviations.)

Guide to respiratory abbreviations.

Abbreviation	Term	Definition
AHI	Apnea–hypopnea index	Total number of apneas and hypopneas per hour of sleep; also see RDI
CPAP	Continuous positive airway pressure	Positive pressure delivered to the upper airway, which splints the airway open and prevents OSA
DLCO	Diffusion in the lung of carbon monoxide	Part of a pulmonary function test to assess gas movement from the alveoli to the erythrocytes, in the pulmonary capillaries. Carbon monoxide is used to make this measurement because it mimics the behavior of oxygen
ERV	Expiratory reserve volume	Maximum volume of air that can be exhaled from the resting end-expiratory level
FEV1	Forced expired volume in 1 s	Volume of air expired in the first second of FVC
FRC	Functional residual capacity	Volume of air remaining in the lungs at end-expiration (RV + ERV)
FVC	Forced vital capacity	Maximum amount of air that can be rapidly and forcefully exhaled from the lungs after full inspiration
RDI	Respiratory disturbance index	Total number of events (apneas, hypopneas, and respiratory effort-related arousals) per hour of sleep; also see AHI
RV	Residual volume	Volume of air remaining in the lungs after maximal expiration, measured indirectly
TLC	Total lung capacity	Total amount of air that the lungs can hold after maximal inspiration
TV	Tidal volume	Amount of air that moves in and out of lungs with each breath

Adapted from C.M. Porth, Essentials of Pathophysiology, third ed., Wolters Kluwer Health/Lippincott Williams & Wilkins, Philapedia, PA, 2011.

Understanding how obesity alters lung function

Alterations in the pulmonary system linked to obesity include abnormalities in ventilatory mechanics and muscle function, ventilatory control, pulmonary gas exchange, and cardiac performance. Signs and symptoms of these problems tend to worsen when an obese patient is supine [2].

Total lung capacity (TLC) and residual volume (RV) are maintained except in cases of extreme obesity, where TLC and RV decrease as weight increases. Most patients maintain a normal forced expired volume in one second/forced vital capacity ratio (FEV1/FVC) in the absence of other lung disease [2,3]. Pulmonary gas exchange (indirectly assessed by measuring the diffusion in the lung of carbon monoxide [DLCO]) may be normal or increased.

Obesity impairs ventilatory function in several ways. As BMI rises, typically all lung volumes are reduced while expiratory airflow remains normal.

Mechanical effects of obesity on the diaphragm and chest wall lead to impaired diaphragmatic excursion and reduced thoracic compliance.

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According to the National Heart, Lung, and Blood Institute, screening for a person's risk of developing obesity-related disease includes calculating the BMI, determining if other conditions associated with obesity (such as a sedentary lifestyle or hypertension) exist, and measuring waist circumference to assess for abdominal fat, which predicts the risk of obesity-associated diseases.

The risk increases for men with a waist circumference larger than 40 inches and women with a waist circumference larger than 35 inches [1].

Factors such as gender, race, age, and height are typically considered when interpreting pulmonary function test results [6]. However, these pulmonary function test results may not be accurate indicators for obese patients because normal predicted values for spirometry, lung volumes, and DLCO usually are not corrected for weight [2,4]. Even though weight is not normally considered when predicting lung values, practitioners must keep in mind that the muscular effort required to support ventilation at rest and during exercise is greater in a patient who is obese than in one of normal weight. This increased muscular effort is due mainly to the higher ventilator requirement brought on by an increased metabolic demand and the increased mechanical loading of the muscles used during inspiration [2].

Let us explore how obesity and decreased lung function are associated with asthma, COPD, and sleep apnea.

Classifying by BMI

Classification	BMI
Underweight	< 18..5
Normal	18.5–24.9
Overweight	25.0–29.9
Obesity Class 1	30.0–34.9
Obesity Class II	35.0–39.9
Extreme Obesity III	⩾40

Source: Centers for Disease Control and Prevention, Obesity and overweight for professionals: health consequences, 2011. http://www.cdc.gov/obesity/causes/health.html.

Obesity and asthma: Increasing together

Asthma is a chronic inflammatory disease that affects the airways [5,6]. Most patients with asthma exhibit increased work of breathing and decreased pulmonary function measurements such as tidal volume (TV), ERV, FEV1, and FVC [7,8].

Rising asthma rates and poor management of the disease are increasingly linked to obesity [7,8].

Females are more likely to have asthma than males [9]. A small percentage of those with asthma may have gained weight because of asthma medications (such as oral corticosteroids) and sedentary lifestyles [7].

Obesity increases the work of breathing and probably exacerbates asthma symptoms caused by the inflammatory process and smooth muscle contraction in the airway [7].

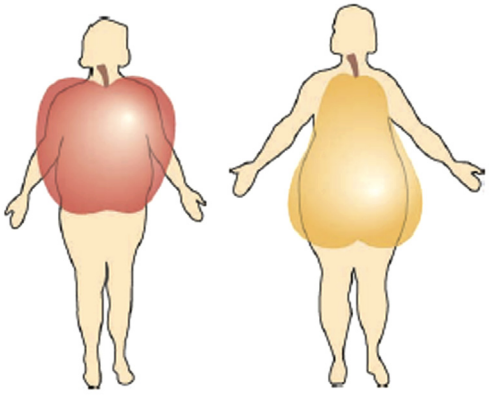
Breathing at low lung volumes could lead to diminished airway stretch (or elasticity). Smooth muscle layers of the conducting airways contain stretch receptors that are affected by pressure changes within the airways. These receptors, which impede inspiration and stimulate expiration, play an essential role in establishing breathing patterns and reducing breathing effort. They do so by making adjustments in the TV and respiratory rate to allow for changes in airway resistance and lung compliance. Reduced airway stretch may create airway hyperresponsiveness, an amplified bronchoconstrictor reaction to stimuli that have minimal to no consequences on others [8,10].

Inflammatory effects

Obesity, a pro-inflammatory condition, increases the number of inflammatory mediators and cytokines such as leptin, tumor necrosis factor alfa (TNF-alfa), interleukin-6 (IL-6), and C-reactive protein (CRP). Airway inflammation contributing to the progression of asthma (or airway hyperresponsiveness) may be promoted by these mediators and cytokines, which are emitted by adipocytes. *Adipocytes* are fat cells in adipose tissue (body fat) that have a cellular volume consisting mostly of pure triglycerides [2]. Upper body (visceral, central, or abdominal) obesity is the main contributing factor in the chronic inflammatory response seen in people who are obese [6]. (See *Comparing apples and pears*.)

Comparing apples and pears

Distribution of adipose tissue in upper body or central (visceral) obesity and lower body or peripheral (subcutaneous) obesity. People with upper body obesity are often considered apple-shaped, while those with lower body obesity are considered pear-shaped.



Source: Porth CM. *Essentials of Pathophysiology*. 3rd ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2011.

Leptin is a protein released by adipocytes that suppresses the appetite by signaling the sensation of satiety and raises energy expenditure. It is also a pro-inflammatory hormone that is greatly increased in obese people with asthma, which stimulates the release of the inflammatory cytokines IL-6 and TNF-alfa [6,7]. IL-6, the chief mediator in acute phase response, leads to the production of CRP, which intensifies the inflammatory response. IL-6 and TNF-alfa are associated with increased IgE production, subepithelial fibrosis, and remodeling of the airways, the primary pathogenesis of asthma [6].

In a recent study of the relationship of inflammatory cytokines of asthma and obesity, Canoz et al., found a positive correlation between biochemical markers (such as erythrocyte sedimentation rate [ESR], CRP, TNF-alfa, and IL-6 levels) and parameters of obesity such as BMI, waist circumference, and waist-to-hip ratio [6].

Management of asthma

The primary goal of asthma treatment is to satisfactorily control the disease to achieve optimal pulmonary function, minimal daytime symptoms and use of rescue bronchodilators, normal activities of daily living, absence of nighttime symptoms, and only mild and infrequent exacerbations. Most patients can achieve satisfactory control with individualized drug therapy, asthma education, environmental control measures, and appropriate follow-up.

Asthma may be more difficult to control in patients who are obese. This difficulty may be associated with factors such as obesity-induced airway changes (for instance, increased airway inflammation and smooth muscle contraction), diminished responsiveness to some medications (such as inhaled corticosteroids and long-acting steroids), or the impact of obesity related comorbid conditions (such as obstructive sleep apnea and gastroesophageal reflux disease [GERD]) [7].

Other associated factors may include the hormonal effects of increased estrogen in females who are obese (it may interfere with the immune response) and worsening of asthma symptoms in obese people with asthma that is linked to theophylline use (which may contribute to GERD by decreasing lower esophageal sphincter tone) [4,8]. Tailored pharmacotherapy is an important management consideration in these patients.

Obesity, smoking, and physical inactivity are modifiable risk factors that can cause or exacerbate asthma [9]. Smoking is also associated with a decreased response to corticosteroids [9].

The key to weight loss is to balance the energy intake with energy expenditure [7]. Exercise training is an effective and safe way for those with asthma to improve fitness and exercise performance. Walking (following U.S. physical activity guidelines) is appropriate even for those with severe asthma [11].

The most dramatic improvements in asthma symptoms occur in morbidly obese patients who have undergone bariatric surgery [7]. Bariatric surgery is typically reserved for severely obese people who are not able to lose weight [12]. These patients, as a result of ineffective nutrient absorption and early satiety produced by intestinal bypass and/or gastric restriction, respectively, loose a significant amount of weight within the first 12 to 18 months after the procedure [13]. Even modest amounts of weight loss are associated with improved asthma severity and control [7].

To further manage symptoms, instruct a patient with asthma to be aware of exercise-induced asthma as physical activity increases and to avoid triggers such as pollen, dust, dust mites, cats, fumes, changes in temperature, and smoke [14].

Obesity and COPD: Raising the risks

COPD, which includes emphysema and chronic bronchitis, is associated with an abnormal inflammatory response of the lungs due to noxious stimuli. These diseases have many common signs and symptoms, such as shortness of breath, cough, exercise intolerance, and airflow limitation that is not completely reversible [15].

The population of patients with COPD is growing as fast as the population of those with obesity [5]. Both conditions are major causes of mortality and morbidity.

Abdominal obesity is about twice as prevalent in patients diagnosed with COPD [2]. The long-term effects of obesity, such as low-grade systemic inflammation and insulin resistance, could also contribute to increased cardiovascular disease and mortality [2].

Most patients with COPD exhibit a nonreversible decrease in FEV1 and FVC (both values are less than 80% of predicted values) along with an FEV1/FVC ratio of less than 70%.

Unlike patients with asthma who have improved lung function with treatment, airflow limitation persists in patients with COPD [4]. The work of breathing and oxygen demand are increased whether these patients are at rest or exercising. With exercise and increased ventilator requirements, these patients may have expiratory flow limitations that can lead to considerable air trapping and an increased end-expiratory lung volume, as reflected in the FRC measurement. Restrictive deficits combined with airflow limitation result in increased shortness of breath and exercise limitations.

In the early stages of COPD, visceral obesity has an especially negative impact on exercise performance [3]. Seres et al. (as reported by Ramachandran et al.) found that diminished exercise ability in patients who were morbidly obese was linked to increases in oxygen requirements, systolic BP, and heart rate. The researchers theorized that these patients with larger body masses required additional energy to create motion due to their diminished exercise ability [3].

Management of COPD

Weight loss is the best health strategy for obese patients with COPD. Cardiac risk factors such as hypertension, diabetes, dyslipidemia, and obesity should be evaluated and managed according to current evidence-based guidelines [3]. Adding pulmonary rehabilitation and exercise training may increase the effectiveness of weight-loss plans and reduce cardiac risk factors [5].

Common therapeutic recommendations include using bronchodilators, supplemental oxygen, inhaled or systemic corticosteroids, antibiotics, and methylxanthines (theophylline) as indicated [16].

- Short-acting bronchodilators such as albuterol and short- or long-acting anticholinergics such as ipratropium or tiotropium are prescribed to relax smooth muscles and improve symptoms.
- Oxygen should be considered for obese patients with hypoxic COPD, as well as those with type 2 diabetes and insulin resistance, because supplemental oxygen increases insulin sensitivity and glucose tolerance [2].

According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, oxygen therapy should be initiated for patients with stage IV COPD. Patients categorized as stage IV have very severe COPD (FEV1/FVC less than 0.70 and FEV1 less than 30% of predicted values, or FEV1 less than 50% of predicted values with chronic respiratory failure).

The GOLD guidelines give the goal for oxygen therapy (resting PaO2 of at least 60 mmHg and/or SaO2 greater than 90% at sea level). According to the GOLD guidelines, the indications for oxygen therapy fall into two categories: first, for those who have a PaO2 of 55 mmHg or less or SaO2 of 88%

or less with or without hypercapnia (a PaCO2 greater than 45 mmHg); second, for those who have a PaO2 55 to 60 mmHg or SaO2 of 88% and show evidence of pulmonary hypertension, pulmonary edema (which suggests heart failure), or a hematocrit greater than 55% [18].

- Inhaled corticosteroids should be given for patients with stage III or IV COPD (severe or very severe) if they are having repeated exacerbations in order to reduce the frequency of exacerbations and reduce airway inflammation (Systemic corticosteroids are recommended only for short-term treatment of exacerbations but not on a long-term basis) [16].
- Antibiotics are useful for patients with COPD who are experiencing infectious exacerbations and/or other bacterial infections, but they should not be used as prophylactic therapy [16].
- Methylxanthines (such as theophylline) have been shown to be effective in COPD as bronchodilators, but due to their adverse reactions and potential toxicity, inhaled bronchodilators are preferred to treat bronchospasm [16]

Besides helping to establish the COPD diagnosis, pulmonary function tests can help assess the patient's response to treatment. A patient with ventilatory failure may need continuous positive airway pressure (CPAP) or endotracheal intubation.

Obesity and obstructive sleep apnea: Common bedfellows

Sleep apnea is defined as the cessation of airflow for at least 10 s corresponding with an arousal from sleep or oxyhemoglobin desaturation [12].

Obstructive sleep apnea (OSA) is characterized by continuing respiratory effort in the face of an absence or serious impairment of airflow. OSA is caused by recurring episodes of upper airway obstruction, usually by the tongue and pharyngeal tissues. During sleep, the muscles of the upper airway relax and the airway opening tends to collapse. As the diaphragm contracts and moves downward to generate negative pressure in the lower airways to inspire air, the upper airway collapses as the tissues and the tongue are sucked into the airway opening. At a minimum, this causes snoring, but it may also cause decreased movement of air (hypopnea) and/or airway obstruction resulting in apnea [17].

The patient is asleep, unaware of this series of events related to breathing, and respiratory efforts continue, although airflow is dramatically reduced or completely stopped.

Hypoxemia and hypercapnia develop, and eventually the patient's sleep moves from a lower level or stage to a higher level (arousal). With this change in brain activity (as measured by electroencephalography), breathing resumes. The hypoxemia and hypercapnia reverse as airflow restarts, but soon the cycle begins again. This pattern recurs throughout the sleep time. Sleep is disrupted by these frequent arousals [20]. Anatomic alterations in people who are obese increase the risk of airway collapse during sleep [15,19].

Risk factors for OSA include obesity, abnormalities in the upper airway and facial structures, and problems related to the soft tissues in the upper airway (such as enlarged tonsils, tongue, or uvula). Potential risk factors for OSA include heredity, smoking, nasal congestion, and diabetes [4]. Significant OSA exists in about 40% of people who are obese, and about 70% of those with OSA are obese. Increased body weight is associated with increased collapsibility of airways in OSA [18].

The total number of apneas and hypopneas per hour of sleep is generally reported as the apnea–hypopnea index (AHI), which is the major index of sleep apnea severity, or the respiratory disturbance index (RDI). OSA is defined as:

- "More than 15 apneas, hypopneas, or respiratory effort–related arousals (RERAs) per hour of sleep (that is, an AHI or RDI greater than 15 events per hour) in an asymptomatic patient, *OR*.
- "More than five apneas, hypopneas, or RERAs per hour of sleep (that is, an AHI or RDI greater than 5 events per hour) in a patient with symptoms (such as sleepiness, fatigue, and inattention) or signs of disturbed sleep (such as snoring, restless sleep, and respiratory pauses). More than 75% of the apneas or hypopneas must have an obstructive pattern" [4].

The consequences of OSA include a host of problems. Frequent interruptions in quality sleep time lead to excessive daytime sleepiness and loss of cognitive function. These patients face an increased risk of severe arterial hypoxemia, higher sympathetic tone, systemic and pulmonary hypertension, cardiac dysrhythmias, heart failure, chronic snoring, cardiovascular disease, and strokes [12,19].

Severe OSA (defined as an AHI greater than 30) carries a three- to sixfold increased risk in all-cause mortality compared to normal people.

Patients with OSA also have more motor vehicle crashes, which are caused when they fall asleep while driving. They are also at higher risk for perioperative problems, such as difficult endotracheal intubation and longer anesthesia recovery time [4].

Although obesity amplifies the risk of OSA, OSA can also promote weight gain and obesity. Studies have shown that many patients newly diagnosed with OSA have recently gained excessive weight.

Management of OSA

The goal of treatment in OSA is to decrease the severity of respiratory events associated with sleep arousal and oxyhemoglobin desaturation [18,19]. CPAP, the treatment of choice for obese patients with OSA, may lower BP and improve endothelial function [5,18]. For a patient with OSA who needs a CPAP mask, ensure that it fits properly.

Evidence supports medical and surgical treatment for weight loss to improve OSA. If weight loss efforts fail, bariatric surgery should be considered [5,13,19]. Bariatric surgery has been shown to reduce patients' BMI by around 15 kg/m^2 and reduces their AHI by 36 events per hour. This suggests that every reduction in BMI of 1 unit is linked to a reduction in the AHI of 2.3 units [20].

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